C1 cont § 119 of European Patent Application No. EP92-402644.6, filed September 25, 1992. –

IN THE CLAIMS

Please cancel claims 30 and 36 without prejudice.

Please amend the claims as follows:

Sub D2 C2 27. (amended) A defective recombinant adenovirus comprising a DNA sequence encoding brain-derived neurotrophic factor (BDNF) [or a derivative thereof], wherein the adenovirus E1 gene is non-functional, and wherein the BDNF sequence is operably linked to a signal controlling expression in cells of the central nervous system.

28. (amended) The [An] adenovirus according to Claim 27, wherein the DNA sequence encodes prepro-BDNF.

29. (amended) The [An] adenovirus according to Claim 27, wherein the DNA sequence is a cDNA sequence.

31. (amended) The [An] adenovirus according to Claim 27, wherein the DNA sequence encodes human prepro-BDNF.

Sub D3 C3 32. (amended) The [An] adenovirus according to Claim 27, wherein the DNA sequence is operably linked to a signal controlling expression in nerve cells.

33. (amended) The [An] adenovirus according to Claim 32, wherein the signal is [selected from the group consisting of] a viral [promoters] promoter [and RSV-LTR promoters].

34. (amended) The [An] adenovirus according to Claim 33, wherein the signal is selected from the group consisting of an RSV-LTR promoter, an [the] E1A promoter, an MLP promoter, and a CMV [promoters] promoter.

35. (amended) A defective recombinant adenovirus comprising a cDNA sequence encoding human prepro-BDNF, operably linked to the RSV-LTR promoter, wherein the adenovirus E1 gene is non-functional.

C4 Sub D4 37. (amended) A defective recombinant adenovirus comprising a DNA sequence encoding human brain-derived neurotrophic factor (hBDNF) [or a derivative thereof] operably linked to a promoter controlling expression in nerve cells, wherein the adenovirus E1 gene is non-functional.

38. (amended) The [A] defective recombinant adenovirus according to Claim 37, wherein the promoter is selected from the group consisting of the neuron-specific enolase promoter and the GFAP promoter.

39. (amended) The [An] adenovirus according to [Claims] Claim 27, lacking regions of its genome which are necessary for replication in a target cell.

40. (amended) The [An] adenovirus according to Claim 39, comprising ITRs and a sequence permitting encapsulation, wherein the E1 gene and at least one of [the] E2, E4 or L1-L5 genes are nonfunctional.

41. (amended) The [An] adenovirus according to Claim 39, wherein said adenovirus is a type Ad 2 or Ad 5 human adenovirus or a CAV-2 type canine adenovirus.

42. (amended) A method for the treatment and/or prevention of a neurodegenerative disease comprising administration of an effective amount of [an] the adenovirus according to Claim 27.

43. (amended) The [A] method according to Claim 42, wherein said disease is selected from the group consisting of Parkinson's disease, Alzheimer's disease, Huntington's disease and ALS.

44. (amended) A pharmaceutical composition comprising the [one or more] defective recombinant adenovirus[es] according to Claim 27.

45. (amended) The [A] pharmaceutical composition according to Claim 44, in injectable form.

46. (amended) The [A] pharmaceutical composition according to Claim 44, comprising between 10^4 and 10^{14} pfu/ml of defective recombinant adenovirus.

47. (amended) The [A] pharmaceutical composition according to Claim 46, comprising between 10^6 to 10^{10} pfu/ml of defective recombinant adenovirus.

48. (amended) A mammalian cell infected with the defective [one or more defective] recombinant adenovirus[es] according to Claim 27.

49. (amended) The [A] cell according to Claim 48, wherein said cell is a human cell.

50. (amended) The [A] cell according to Claim 49, wherein the cell type is selected from the group consisting of fibroblast, myoblast, hepatocyte, endothelial cell, glial cell and keratinocyte.

52. (amended) The [An] implant according to Claim 51, wherein the extracellular matrix comprises a gelling compound selected from the group consisting of collagen, gelatin, glucosaminoglycans, fibronectin and lectins.

53. (amended) The [An] implant according to Claim 51, wherein the extracellular matrix comprises a support permitting anchorage of the cells.

54. (amended) The [An] implant according to Claim 53, wherein the support comprises polytetrafluoroethylene fibres.

REMARKS

Claims 27-29, 31-35, and 37-54 are pending in the application. All of the claims have been amended to particularly point out and distinctly claim that which Applicants regard as the invention, e.g., to correct typographical and editing errors, to state singular number where appropriate, and to reflect dependency by use of the definite article where appropriate. Support for amended claims 27, 35, and 37 can be found in the specification, e.g., at page 10, lines 2-9 and page 24, lines 10-13 (adenovirus with E1 rendered non-functional). Further support for the amended recitation of claim 27 is found at page 9, lines 4-5 (expression of BDNF in cells of the central nervous system).

The Restriction Requirement Is Improper

The Examiner has deemed proper and made final the restriction requirement. The Examiner improperly contends that Barde (US Patent No. 5,180,820; hereinafter "Barde") teaches a defective recombinant adenovirus encoding BDNF. For the reasons pointed out previously, Barde fails to teach an adenovirus of the invention. To further clarify this issue, Applicants have amended claims 27, 35, and 37 to recite that the adenovirus vector lacks the E1 region, a characteristic with respect to which Barde is totally silent. The instant specification clearly speaks to this issue:

- at page 9, lines 11-28, the specification states that the adenovirus vector comprises the ITRs, encapsidation sequence, and BDNF, and that in such a vector, the E1 region (and one or more other regions) are rendered non-